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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/600,129	06/19/2003	Sarah S. Bacus	6155-US-NP	9778

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EXAMINER	
HOLLERAN, ANNE L	

ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/600,129	BACUS ET AL.	
	Examiner	Art Unit	
	ANNE L. HOLLERAN	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 May 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30 and 33-38* is/are pending in the application.

4a) Of the above claim(s) *1-28 and 35-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29, 30, 33 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 5/13/2010 is acknowledged.

Claims 1-30, and 33-38 are pending. Claims 1-28 and 35-38, drawn to non-elected inventions, are withdrawn from consideration.

Claims 29, 30, 33 and 34 are pending and examined on the merits.

Claim Rejections Maintained and New Grounds of Rejection:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29, 30, 33 and 34 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 is indefinite because it is not clear what the metes and bounds of "an optical density less than 9" for a quantitative immunohistochemistry assay. It is not clear from the specification whether the cut-off of 9 for optical density is dependent on the particular assay used in the working embodiments, and also whether this optical density cut-off is specific to the particular equipment for measuring optical density used in the working embodiments.

Applicants state that optical density is a fairly routine measurement that can readily be carried out by one skilled in the art and that the claims should not be limited to a specific assay or equipment type in order to specifically point out and claim the invention.

The rejection is maintained because neither the specification nor applicants' arguments correlate the optical density of 9 with measurements an expression level of HER3 in cells from a cancer, using any anti-Her3 detection system in a quantitative immunohistochemistry assay. It is not clear what the optical density of 9 corresponds to in terms of amount of HER3. Sompuram (Sompuram, S.R., et al., The Journal of Histochemistry & Cytochemistry 50(11): 1425-1433, 2002.) teaches an example where optical density is measured on a 0-2 scale (page 1429, legend of Figure 5). Sompuram also teaches that standardization of quantitative IHC (immunohistochemistry) has been hampered by a lack of internationally agreed-on reference standards and calibrators (see page 1431, right column). Therefore, the rejection is maintained for the reasons of record.

Claim 29 is newly found to be indefinite because of the amendment adding the step of further assaying a cell or tissue sample from the subject to detect an expression level for one or more of HER1 (EGFR), pHER1, HER2/neu, and pERK in cells from the cancer. It is not clear how this step results in a method of treating a subject, because this step is not associated with the selection step of treating a subject with an anti-EGFR antibody when the detected HER3 expression level is detected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 29 and 33 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Hudziak (US 5,770,195; issued Jun. 23, 1998) in view of Esteva (Esteva, F. J. et al., Pathology Oncology Research, 7(3): 171-177, 2001), in view of Pinkas-Kramarski (Pinkas-Kramarski, R. et al, Oncogene, 16: 1249-1258, 1998), and further in view of Hoffmann (Hoffmann, M., et al., Cancer Immunol. Immunother., 47(3): 167-175, 1998; abstract only).

Applicants state that none of the cited references either alone or in combination teach or suggest the instantly claimed methods. Applicants state that Hudziak does not disclose the existence of HER3 or its use as a biomarker. Applicants state that Esteva fails to disclose or suggest that any of the biomarker patterns of expression could be used to select a subject for treatment with a molecule targeting EGFR; that Pinkas-Kramarksi does not teach or suggest treatment with any therapy, much less a therapy base on anti-EGFR antibody as required by the

present claims; and that the deficiencies of Hudziak, Esteva or Pinkas-Kramarski cannot be overcome by combination with Hoffmann, which relates the expression of receptors such as ErbB-2 (HER2) and ErbB-3 (HER3) with TNF-alpha insensitivity. Applicants conclude that one skilled in the art would not have been motivated to arrive at the instant invention.

Applicants' arguments have been carefully considered, but fail to persuade. The amendment includes the detection of HER2/neu, which is a known coreceptor with HER3; the amendment includes the detection of HER1 (EGFR), which is the receptor targeted by an anti-EGFR antibody. Applicants state that the combination of references does not motivate one of skill in the art to arrive at the instant invention. However, it appears that applicant is narrowly construing the claims to be limited to selecting a subject based on HER3 expression level. The claims are broader than this because the claims comprise treating a subject with low HER3 expression level. Therefore, the claims read on a method with three steps: measuring HER3 levels, treating a subject with low HER3 levels with an anti-EGRF antibody (which encompasses treating a group of subjects where a subset happen to have low HER3 levels) and measuring levels of HER1 (EGFR), pHER1, HER2/neu, or pERK. As stated in the previous Office action, the prior art suggests a method comprising administering an anti-EGFR antibody to a population of patients with a low Her3 level because the prior art teaches that both EGFR growth pathways, as well as Her2/Her3 (ErbB2/ErbB3) pathways are known to contribute to growth and survival of cancers. Therefore, targeting cancers where one pathway activity is low, i.e. ErbB2/ErbB3 pathway, which would be determined by measuring expression levels of ErbB3. Additionally, this pathway could be measured by detecting levels of ErbB2 (HER2/neu). Therefore, the rejection is maintained for the reasons of record.

Claims 29, 30, 33 and 34 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Hudziak (US 5,770,195; issued Jun. 23, 1998) in view of Esteva (Esteva, F. J. et al., Pathology Oncology Research, 7(3): 171-177, 2001), in view of Pinkas-Kramarski (Pinkas-Kramarski, R. et al, Oncogene, 16: 1249-1258, 1998), in view of Hoffmann (Hoffmann, M., et al., Cancer Immunol. Immunother., 47(3): 167-175, 1998; abstract only), and further in view of Yang (Yang, X.-D. et al., Critical Reviews in Oncology/Hematology, 38: 17-23, 2001).

Applicants state that Yan simply adds recitation of ABX-303 antibody, and that the combination of Yang with Hudziak, Esteva, Pinkas-Kramarski and Hoffmann does not suggest of render obvious the claim limitations.

For the reasons stated above, neither the amendment nor applicants' arguments obviate the rejection of record because the motivation to combine the references to arrive at the claimed invention does not have to be the same as applicants' reasons for making the claimed invention. Therefore, the rejection is maintained for the reasons of record.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
/Alana M. Harris, Ph.D./

Primary Examiner, Art Unit 1643